

10/527594

DT15 Rec'd PCT/PTO 14 MAR 2005

Docket No.: 1173-1027P
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Amy NEWMAN et al.

Application No.: Not Yet Assigned

Confirmation No.: N/A

Filed: March 14, 2005

Art Unit: N/A

For: STRUCTURALLY RIGID DOPAMINE D3
RECEPTOR SELECTIVE LIGANDS AND
PROCESS FOR MAKING THEM

Examiner: Not Yet Assigned

LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The PTO is requested to use the amended sheets/claims attached hereto (which correspond to Article 34 amendments during prosecution of the above-identified national phase PCT application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §1.16 or 1.14; particularly, extension of time fees.

10/527594

DT15 Rec'd PCT/PTO 14 MAR 2005

Application No.: Not Yet Assigned

Docket No.: 1173-1027P

Dated: March 14, 2005

Respectfully submitted,

DRN/clb

By Ma Cu 13,040,661

Mark L. Nuell

Registration No.: 36,623

BIRCH, STEWART, KOLASCH & BIRCH, LLP

8110 Gatehouse Rd

Suite 100 East

P.O. Box 747

Falls Church, Virginia 22040-0747

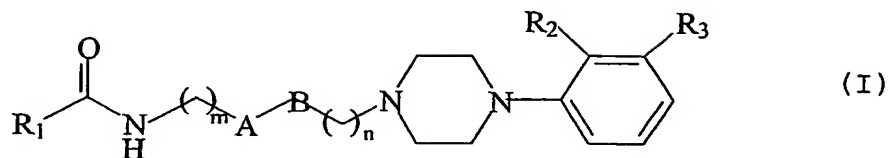
(703) 205-8000

Attorney for Applicant

Attachment(s)

We claim:

1. A compound having the formula



wherein

5 A is cis or trans -CH=CH-, -C≡C-, or cyclohexyl;

B is cis or trans -CH=CH- or absent;

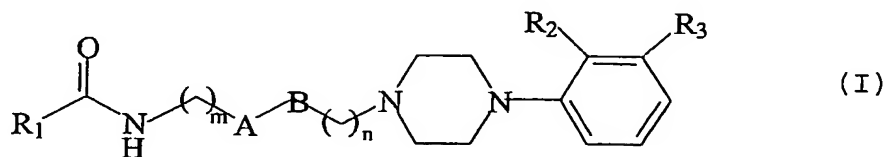
R₁ represents an optionally substituted phenyl group, wherein said substituents are selected from the group consisting of: hydrogen, halogen, amino, nitro, hydroxyl, alkoxy, alkyl, acyl
10 and pyridyl, and said substitution may occur at any of the ortho, meta, or para positions, or R₁ represents a heteroaromatic ring;

R₂ and R₃ may be independently hydrogen or a halogen, or R₂ alone may be C₁, C₂, or C₃ alkoxy;

15 m is 1 or 2; and

n is 0, 1, or 2.

2. A compound having the formula



20 wherein

A is cis or trans -CH=CH-, -C≡C-, or cyclohexyl;

B is cis or trans -CH=CH- or absent;

R_1 represents an optionally substituted phenyl group, with the exception that R_1 is not triazole or thiadiazole, wherein said substituents are selected from the group consisting of: hydrogen, halogen, amino, nitro, hydroxyl, alkoxy, alkyl, acyl and pyridyl, and said substitution may occur at any of the ortho, meta, or para positions, or R_1 represents a heteroaromatic ring;

R_2 and R_3 may be independently hydrogen or a halogen, or R_2 alone may be C_1 , C_2 , or C_3 alkoxy;

m is 1 or 2; and

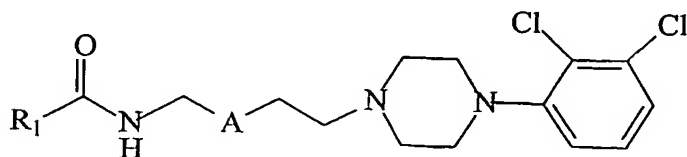
n is 0, 1, or 2.

3. The compound of claim 1, wherein B is absent, R_2 and R_3 are both halogen, m is 1 and n is 1.

4. The compound of claim 1, wherein B is absent, R_2 is lower alkoxy, R_3 is H, m is 1 and n is 1.

5. The compound of claim 1, wherein R_1 is phenyl substituted by a halogen, an amino group, a nitro group, a methoxy group, or pyridyl group.

6. A compound having the formula:



wherein

A is cis or trans -CH=CH-, -C≡C-, or cyclohexyl; and

R₁ represents an optionally substituted phenyl group, with the exception that R₁ is not triazole or thiadiazole, wherein
5 said substituents are selected from the group consisting of: hydrogen, halogen, amino, nitro, hydroxyl, alkoxy, alkyl, acyl and pyridyl, and said substitution may occur at any of the ortho, meta, or para positions, or R₁ represents a heteroaromatic ring.

10

7. A method of treating cocaine abuse in a subject, comprising the steps of:

administering to the subject an amount of a compound of claim 1 effective to inhibit binding of dopamine to a dopamine
15 D3 receptor in the brain of said subject.

8. A method for selectively imaging dopamine D3 receptor in the central nervous system of a subject, comprising:

(a) administering a radioactively labeled compound of
20 claim 1 to the subject; and

(b) detecting the binding of that compound to dopamine D3 receptors in the central nervous system of the subject.

9. A method for detecting or monitoring a disease
25 resulting from abnormal distribution and/or density of

dopamine D3 receptor in the central nervous system of a subject, comprising:

(a) administering to the subject a detectably labeled compound of claim 1;

5 (b) detecting the binding of that compound to dopamine D3 receptor in the central nervous system tissue;

(c) determining the distribution and/or density of the dopamine D3 receptor in the central nervous system tissue;

(d) comparing the distribution and/or density obtained in
10 (c) with the distribution and/or density of dopamine D3 receptor in a corresponding normal tissue; and

(e) diagnosing a disease state by a difference in the distribution and/or density between the normal tissue and the subject tissue.

15
10. The method of claim 8 or 9, wherein the central nervous system tissue is brain tissue.